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LETTERS AND CORRESPONDENCE

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Improvement of Erythropoiesis During Treatment With Deferiprone In a Patient With Myelofibrosis and Transfusional Hemosiderosis

To the Editor: Transfusional hemosiderosis can successfully be treated with desferrioxamine (DFO), subcutaneously or intravenously. Compliance, however is poor. New oral iron chelators such as Deferiprone (L1: 1,2 dimethyl-3-hydroxpyrid-4-one) have proven to be effective, but side effects such as agranulocytosis, arthralgias, and dyspepsia are not negligible [1].

In 1986 a 42-year-old man was admitted with a normocytic, normochromic anemia [hemoglobin (Hb): 6 g/dl]. Physical examination revealed splenomegaly and mild hepatomegaly, no lymphadenopathy. Ferritin, vitamin B12, folate, platelets, and white blood cells (WBC) were normal. The diagnosis myelofibrosis was established by bone marrow biopsy. Despite therapy with folate and vitamin B12, blood transfusions, two units of red cells (URC) 2 weekly were necessary to keep his Hb level over 9.6 g/dl. In December 1987 a splenectomy was performed because of pancytopenia, increasing blood transfusion requirements, and progressive splenomegaly. For almost one year the Hb stabilised and no blood transfusions were necessary. Thereafter the blood transfusion requirements increased again to two URC 2 weekly. In June 1990 the patient was found to have slightly impaired liver functions and ferritin level of 13,497 μg/l (reference value 90–100 μg/l). Computer tomography scanning of the liver confirmed the diagnosis hemosiderosis. We started treatment with 3 g DFO infusions during 10 h subcutaneously, 3 times a week. Urinary iron excretion (UIE) increased to maximal 29 mg/24 h. During this treatment transfusion requirements were unchanged and no significant decrease of the ferritin level was observed.

Because of poor compliance, treatment with the oral iron chelator L1 50 mg/kg/day divided in three doses was started in September 1992. After 1 month treatment, surprisingly, an increase of the Hb level was seen and the

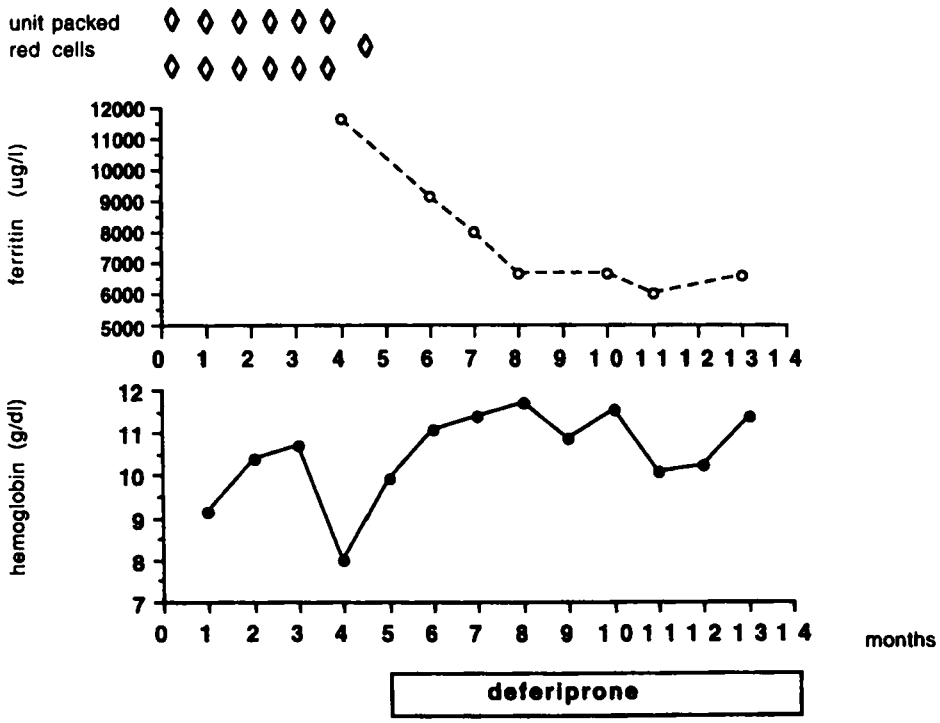

Fig. 1. Ferritin level.

patient no longer required blood transfusions. UIE increased to maximally 15.6 mg/24 h. A sharp decrease in ferritin level was observed (Fig. 1).

Increasing erythropoiesis during iron chelating therapy with DFO has been noticed in a number of studies. In patients with myelodysplastic syndrome as well as myelofibrosis, a reduction in blood transfusion needs was observed during treatment with DFO [2]. The response to recombinant erythropoietin, in patients with anemia of end stage renal failure and hemosiderosis, was improved by DFO. In patients with rheumatoid arthritis, a rise of Hb was observed during treatment with DFO and L1. Although aluminum chelating effects or reduction of disease activity cannot be excluded, ferrokinetic changes can explain the response [3].

After mobilisation of iron from the iron stores, not only iron excretion in urine is increased, but it may also be redistributed to the hematopoietic tissues by the chelator itself or by exchanging it with transferrin. In vitro studies have demonstrated that DFO can stimulate transferrin receptor expression on the erythroblast [4]. It has also been shown that iron chelators can pass the erythroblast membrane [5].

Before starting treatment with L1 our patient required about two to four URC each month. Repeated bone marrow biopsy showed no changes. We believe that iron kinetic changes due to L1 can possibly explain the observed phenomenon in our patient.

In view of these speculations, further research of the pharmacokinetics and effects of L1 and other iron chelators on iron metabolism and iron (re)distribution is necessary.

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Granulocytic Sarcoma of the Uterus Complicating Myelodysplastic Syndrome

To the Editor: Myelodysplastic syndrome (MDS) is a clonal disorder characterized by ineffective hemopoiesis and myelodysplasia [1]. The patients often present with complications of pancytopenia and the disease may terminate in acute myeloid leukemia (AML). The latter usually evolves through a gradual rise of blast count in the peripheral blood and bone marrow. Rarely, patients with MDS may develop tumorous masses of immature myeloid cells (granulocytic sarcoma), with or without concomitant systemic involvement [2]. We report a patient with MDS complicated by granulocytic sarcoma of the uterus. The latter heralded the development of frank leukemia.

A 35-year-old female presented with gum bleeding and menorrhagia in August 1993. Peripheral blood counts showed: hemoglobin 11.2 g/dL, platelets 12×10^9/L, and leukocytes 5.9×10^9/L with 55% neutrophils, 16% lymphocytes, 2% monocytes, 2% eosinophils, 4% basophils, 2% metamyelocytes, 4% myelocytes, 2% promyelocytes, and 13% Auer rod-containing blast cells. The neutrophils showed pseudo-Pelger Huet anomaly. The marrow was hypercellular with reduced megakaryocytes, megaloblastoid erythropoiesis and abnormal granulopoiesis with around 20% blast cells (500-cell differential count on separate occasions). Cytogenetic studies performed by culturing of the marrow cells revealed 45-46,XX,t(8;21)(q22;q22),del(9)(q11q22)(15). A diagnosis of refractory anemia with excess of blasts in transformation was made according to the FAB classification, although in the presence of t(8;21), this could well represent, biologically, an evolving phase of AML (M2) [3].

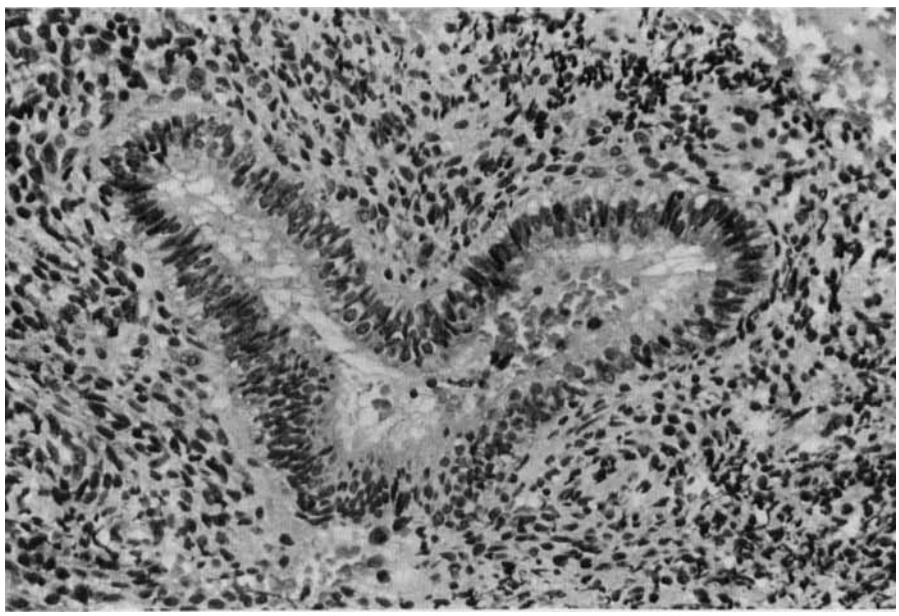

Fig. 1. Endometrial biopsy showing a compact infiltrate of myeloblasts in the endometrium (hematoxylin & eosin, ×160).